REMARKS

Claims 21-63 are currently pending in the present application. No amendments have been made in this Request for Reconsideration.

A. The Rejection

The sole outstanding rejection in the above-identified application is a rejection of claims 21-63 under 35 U.S.C. §112, first paragraph, as containing subject matter which is not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

In the Advisory Action dated February 24, 2005, the following statement was made,

> These documents [Margot et al. and Brun-Verzinet et al. submitted on November 3, 2004] have been considered on their merit by the Examiner, however, [these documents] are indicated as being post-filing art. In the absence of art or factual evidence at the time the invention [sic – application] was filed regarding the instant application, one skilled in the art would be unable to derive rules for the rules database and thus the invention is considered not enabled.

The applicant finds this statement very surprising since it appears to indicate that, according to the Examiner, there is no evidence of record regarding the enablement of the invention at the time the above-identified application was filed. However, this is clearly incorrect. The correct state of the record in the present application is detailed below for the convenience of the Examiner.

B. The Evidence Presented by the Examiner in Support of the Enablement Rejection

None

C. The Evidence Presented by the Applicant Demonstrating Enablement

1. "CTSHIV: A Knowledge-Based System for the Management of HIV-infected Patients," Pazzani et al., *Proceedings: Intelligent Information Systems, IIS' 97* (CAT. No. 97TB100201), 1997, pages 7-13 (hereinafter "Pazzani et al."),

2. "Knowledge-Based Avoidance of Drug-Resistant HIV Mutants," Lathrop et al., *American Association of Artificial Intelligence*, 1998, pages 1071-1078 (hereinafter "Lathrop '98").

3. Declaration of Charles Boucher, PhD,

4. Declaration of Andrea de Lucia, M.D.,

5. "Genotypic and phenotypic analyses of HIV-1 in antretroviral-experienced patients treated with tenofovir DF," Margot, N.A., et al., *AIDS*, 2002, **16**:1227-1235, and

6. "Clinically relevant interpretation of genotype for resistance to abacavir," Brun-Vézinet, F. et al., *AIDS*, 2003, **17**:1795-1802.

Thus, it can be seen that there are four pieces of evidence, items (1)-(4) above, of record, that present factual evidence demonstrating enablement of the claimed invention at the time that the present application was filed, and that there are two additional pieces of evidence (5)-(6), of record, that were used at the personal interview to demonstrate how a skilled person implements various aspects of the present invention, without undue experimentation. There is no evidence in the record that has been offered for the purpose of (1) supporting the Examiner's enablement rejection, or (2) to rebut the voluminous evidence that has already been made of record by the applicant.

D. The Invention

Applicant claims a method for effecting computer implemented decision-support in selection of a drug therapy, whereby a rules database is used. The rules database used by the method of the present invention comprises a number of associated rules for each available drug used in treatment of a viral disease, with each rule used to give an indication the suitability of the drug for treatment of a specific viral genotype, based on a resistance level and a confidence level. See specification page 1, lines 16-30.

E. The Derivation of Rules for the Claimed Rules Database

1. The Examiner's Position

The Examiner raises several objections, all of which are based on the Examiner's position that the present specification does not give a detailed description of exactly how to derive each rule in the rules database. The applicant, however, has demonstrated, with extensive evidence, that either: (1) the specification does, in fact, describe exactly how to derive some of the rules in the rules database, and (2) that it is not necessary for the specification to described how to derive the other rules in the rules database because those rules were already in existence at the time the present application was filed. See e.g. MPEP Section 2164.05(b).

In the Final Rejection at the bottom of page 6, the Examiner has taken the position that,

> Absent [from the specification] is the manner/procedures the core-committee review [sic – reviews] publications, assigns resistance level and confidence level to derive a suitability value, and the parameters that define the decision process so that adjustments can be made to the "rules".

2. Assignment of Confidence Level

The applicant has demonstrated that a skilled person can assign a confidence level by following the clear teachings of the present specification. Moreover, the skilled person does not require any information beyond what is contained in the specification to carry out this aspect of the present invention. With regard to the assignment of confidence level, the specification teaches as follows:

> The second value assigned to each drug is indicated as confidence level indicating how much support there is for this result in the scientific literature. A confidence value has one of the following levels:
>
> (1) suggestive evidence,
> (2) proven in vitro,
> (3) proven in vivo.

See specification at page 5, line 35 to page 6, line 6. Therefore, to assign a confidence level, the skilled person need only review a publication and determine if the information contained in the publication was obtained (a) in vitro, (b) in vivo, or (c) via some other method. Once this determination is made, the skilled person then assigns a confidence level of "(3)" if the information was obtained in vivo, a confidence level of "(2)" if the information was obtained in vitro, or a confidence level of "(1)" if the information was obtained via some other method. Clearly, a skilled person is capable of assigning a confidence level based on this teaching of the specification without any experimentation whatsoever.

3. Assignment of Resistance Level

The applicant has demonstrated that a skilled person is capable of assigning a resistance level using either or both of: (1) knowledge contained in the prior art, and (2) the common general knowledge of a person of ordinary skill in the art. The Examiner has presented no evidence to rebut the significant body of evidence that the applicant has submitted in relation to this issue.

With regard to assignment of the resistance level, the specification teaches as follows:

> The first value is indicated as the resistance level providing information on how much resistance is conferred on the drug by this substitution. The resistance level is represented on a scale from 0 (low resistance) to 3 (high resistance).

See page 5, lines 6-11 of the specification.

According to the declarations of Charles Boucher, PhD, and Andrea de Lucia, M.D., the publications relied on by the applicant, namely, Lathrop '98 and Pazzani et al., demonstrate that a skilled person already knows how to assign a resistance level of the genotype for a drug using the then-existing CTSHIV system. See paragraphs 7-11 of each of the declarations.

Specifically, Lathrop '98 teaches as follows:

> Current drug resistance is identified by applying the 55 rules in the [CTSHIV] knowledge base to the HIV sequences from the patient. The rules represent knowledge about HIV drug resistance as a set of if-then rules of the form:
>
> IF (antecedent) THEN (consequent) [weight].
>
> For example, one such rule in CTSHIV is:
>
> IF Methionine is encoded by RT codon 151, THEN do not use AZT, ddI, d4T, or ddC. [weight= 1.0]
> (Iverson et al. 1996).
>
> The weight associated with a rule is not a confidence as in many expert systems. Rather, it reflects the estimated level of resistance to a particular drug, and is part of the consequent. Weights range from 0.1 (low) to 1.0 (high) based upon expert advice and the level of resistance reported in the literature.

See Lathrop '98 at pages 1073-74 under the heading, "Identify Current Resistance." From this portion of Lathrop '98 it is clear that as of 1998:

(1) the CTSHIV knowledge base was already in existence,

(2) by 1998, the CTSHIV knowledge base already contained 55 rules for determining HIV drug resistance levels based on genotype,

(3) The 55 rules reflected the estimated level of resistance to a particular drug, as is the case for the resistance level of the present application,

(4) The 55 rules were based upon expert advice and the level of resistance reported in the literature, as is the case for the resistance level of the present application, and

(5) Weights range from low to high on a numerical scale, as is the case for the resistance level of the present application.

Thus, the evidence of record clearly shows that a skilled person, as of 1998, was capable of assigning a resistance level using the then-existing CTSHIV knowledge base and the 55 rules for assigning resistance level contained therein. According to MPEP §2164.01:

> ("The test of enablement is whether one reasonably skilled in the art could make or use the invention from the disclosures in the patent **coupled with information known in the art without undue experimentation.**"). **A patent need not teach, and preferably omits, what is well known in the art.** *In re Buchner*, 929 F.2d 660,661, 18 USPQ2d 1331,1332 (Fed.Cir. 1991); *Hybritech,Inc.v.Monoclonal Antibodies ,Inc .*, 802 F.2d 1367,1384, 231 USPQ 81,94 (Fed.Cir. 1986), *cert.denied*, 480 U.S.947 (1987); and *Lindemann Maschinenfabrik GMBH v. American Hoist & Derrick Co.*, 730 F.2d 1452,1463, 221 USPQ 481, 489 (Fed.Cir.1984). (Emphasis added).

The applicant has clearly demonstrated that the CTSHIV knowledge database was known in the art as of 1998 and that the CTSHIV knowledge database provides a method for assigning a resistance level in accordance with the teachings of the present specification. Thus, as stated above in MPEP §2164.01, the specification need not teach, and preferably omits, that which is well known in the art, i.e. the CTSHIV knowledge database.

The Examiner has not provided any evidence or reasoning showing why a skilled person cannot assign a resistance level using the CTSHIV knowledge database of Lathrop '98 and Pazzani et al. Thus, the evidence of record, overwhelmingly shows that the skilled person could assign a resistance level in accordance with the present claims using the CTSHIV knowledge base at the time of filing of the present application.

Finally, as stated in the declarations of Charles Boucher, PhD, and Andrea de Lucia, M.D., the rules database of the present invention may be merely a codification of the decision-making process that is already used every day by clinicians throughout the world to determine proper drug therapy. See e.g. paragraph 8 of each of the Declarations. More specifically, as of the filing date of the present application, clinicians were prescribing drug therapy for HIV patients every day without the need to consult the present patent specification. Instead, these clinicians employ at least their experience, common general knowledge, diagnosis, and knowledge of the medical literature to make these decisions. Also, the clinicians apply certain rules in the decision-making process to determine the weight to give to each piece of information in the final decision. Although the rules are applied in the brain of the clinician, the clinician is capable of elucidating these rules and thereby creating the database for use in the present invention.

Therefore, since the provision of a rules database can be carried out by skilled persons using their common general knowledge, and, in actual fact, was carried out by clinicians every day as of the filing date of the present application, there is no need for the specification of the present application to disclose, in detail, a specific algorithm/step/procedure for creating a specific rules database. The claims cover any method for assigning these values that involves use of the information specified in the claims, and all of the evidence of record supports the conclusion that a skilled person, exercising common general knowledge, is capable of assigning these values without requiring further guidance from the present application.

4. Deriving a Suitability Indication

The applicant has demonstrated that a skilled person can derive a suitability indication from the assigned confidence and resistance levels by following the clear teachings of the present specification. With regard to the derivation of a suitability indication, the specification teaches as follows:

> In applying the rules database, for each PI or NRTI drug, where one of [sic – or] more rules apply, the suitability level is the maximum of all levels derived. For each NNRTI drug, where more than one rule applies, the suitability level is the sum of all levels derived, up to a maximum of 3.

See the specification at page 7, line 16 to page 8, line 2. From this, it is apparent that there are two different situations for deriving a suitability indication:

(1) For a PI or NRTI drug, or

(2) for a NNRTI drug.

For situation (1), a PI or NRTI drug, the skilled person need only determine which of the confidence level or the resistance level is the highest, and that value becomes the suitability indication. Surely, a skilled person is capable of looking at two numbers on a scale of 0 to 3 (i.e. the confidence and resistance levels), determining which of the numbers is higher, and picking the higher number to derive the suitability indication for situation (1). Seven examples of deriving the suitability indication in this manner are given in the table at lines 5-6 of page 7 of the specification.

For situation (2), a NNRTI drug, the skilled person need only add up the values of the confidence and resistance levels and then derive a resistance value by taking either: (1) the sum of the values of the confidence and resistance levels, if that sum is less than or equal to 3, or assigning a suitability indication of 3 if the sum of the confidence and resistance levels is greater than 3.

Surely, a skilled person is capable of carrying out such simple mathematical manipulations. Five examples of deriving a suitability indication for situation (2) are given in the table between lines 14 and 15 of page 7 of the specification.

5. Conclusions

From the foregoing, it is absolutely clear that, contrary to the Examiner's assertions, the specification clearly teaches how to assign a confidence level, the skilled person already knew how to assign a resistance level at the time of filing the present application using the CTSHIV knowledge base, and the specification teaches that elementary arithmetic can be employed to derive a suitability indication once the confidence and resistance levels are assigned.

F. Additional Positions Taken by the Examiner

The Examiner has also taken the following positions at pages 4-5 of the Final Rejection,

> With respect to the instant claims, Pazzani et al. and Lathrop et al. [Lathrop '98] fail to teach: 1) the suitability indication to be based on at least a combination of a first value (resistance level) and a second value (confidence level); 2) displaying a ranking which includes both the individual drugs and certain combinations of drugs displayed together; 3) based on at least a first value indicating the resistance level of the genotype for the drug when present at a certain drug level in a patient; and 4) the use of the clade of a virus in selecting a suitable drug therapy. The instant specification does not cure the deficiencies of Pazzani et al. and Lathrop et al. [Lathrop '98] for the claimed invention.

The applicant will address each of these concerns, in turn, below.

1. The Suitability Indication

The Examiner takes the position that neither Pazzani et al. nor Lathrop '98 teaches that the suitability indication is to be based on at least a combination of the resistance level and the confidence level and that the instant specification does not cure the deficiencies of Pazzani et al. and Lathrop '98. This is clearly incorrect since the specification teaches that the suitability indication is to be based at least on a combination of the resistance level and the confidence level at page 6, lines 8-11. Moreover, as discussed in Section E.4 above, the specification also teaches exactly how to derive the suitability indication from the combination of resistance level and confidence level using elementary mathematics at page 7, line 16 to page 8, line 2. Thus, contrary

to the Examiner's assertion, the present specification clearly cures the deficiencies of Pazzani et al. and Lathrop '98 with respect to the derivation of the suitability indication.

2. Displaying a Ranking of Individual Drugs and Drug Combinations Together

The Examiner takes the position that neither Pazzani et al. nor Lathrop '98 teaches the display of a ranking of individual drugs and drug combinations together and that the instant specification does not cure the deficiencies of Pazzani et al. and Lathrop '98. This is clearly incorrect since the specification includes an example of a display of just such a ranking at page 7, between lines 5 and 6. In this ranking, "IND" is an example of an individual drug displayed in the ranking, whereas "IND (+RTV)" is an example of a drug combination displayed in the ranking. The specification also contains a detailed description of how to arrive at this ranking using the existing knowledge of a skilled person on pages 6-8, as discussed in detail in Sections E.2-E.4 above. Thus, contrary to the Examiner's assertion, the present specification clearly cures the deficiencies of Pazzani et al. and Lathrop '98 with respect to the display of a ranking of individual drugs and drug combinations together.

3. Ranking Based on the Resistance Level of the Genotype for the Drug When Present at a Certain Drug Level

The Examiner takes the position that neither Pazzani et al. nor Lathrop '98 teaches the display of a ranking of drugs and drug combinations based on the resistance level of the genotype for the drug when present at a certain drug level and that the instant specification does not cure the deficiencies of Pazzani et al. and Lathrop '98. This is clearly incorrect since the specification includes an example of a display of just such a ranking at page 7, between lines 5 and 6.

Specifically, referring to the table at page 7, between lines 5 and 6 of the specification, it can be seen that this table displays a ranking of drugs and drug combinations based on a suitability indication. The drugs and drug combinations are given in the column entitled, "drug", and the suitability indication is given in the column entitled, "suitability." Moreover, the genotype is given in the column entitled, "substitution", the resistance level is given in the column entitled, "resistance", and the drug level is given in the column entitled, "level."

Thus, contrary to the Examiner's assertion, the present specification clearly cures the deficiencies of Pazzani et al. and Lathrop '98 with respect to the display of a ranking of individual

drugs and drug combinations based on the resistance level of the genotype for the drug when present at a certain drug level.

4. The Use of the Clade of the Virus to Select a Suitable Drug Therapy

The Examiner takes the position that neither Pazzani et al. nor Lathrop '98 teaches the use of the clade of the virus to select a suitable drug therapy and that the instant specification does not cure the deficiencies of Pazzani et al. and Lathrop '98. This is clearly incorrect since the specification includes the following teaching at page 9, lines 6-13:

> Further data to be entered may comprise information on the viral load, the CD4 cell count, if known, and the clade classification.... The clade information can be used in selecting a drug therapy.

Thus, contrary to the Examiner's assertion, the present specification clearly cures the deficiencies of Pazzani et al. and Lathrop '98 since it contains a teaching to use the clade of the virus to select a suitable drug therapy.

As to how the clade of the virus is used to select a suitable drug therapy, the specification need not teach this feature since it is well known to persons of ordinary skill in the art. See e.g. paragraphs 23-24 of the Declarations of Charles Boucher, PhD, and Andrea de Lucia, M.D. These declarations explain that if a skilled person desires to use the clade of a virus to select a suitable drug therapy, the skilled person simply specifies the clade of the virus for the patient to be treated and only information relevant to the specified clade will then be considered. In other words, the skilled person already knows that the clade of a virus is used to exclude data from consideration if such data does not relate to the specified clade. It is as simple as that.

5. Conclusion

Accordingly, from the foregoing discussion it is clear that the Examiner's position is unsupported by evidence and that the evidence of record persuasively rebuts each of the Examiner's specific objections.

G. The Examiner's Request That the Applicant Demonstrate the Invention

On page 8 of the Final Rejection, the Examiner asked the applicant to demonstrate the invention using two references cited by the Examiner, namely, the Dunn et al. and Lewis et al. references. At the personal interview of November 1, 2005, the applicant pointed out that the

Dunn et al. and Lewis et al. references do not relate to the viral resistance of HIV to drugs or drug combinations and do not provide genotype information. Thus, the skilled person would not consider either of the Dunn et al. and Lewis et al. references in the implementation of the present invention since these references do not provide information relevant to the viral resistance of HIV to drugs or drug combinations, and these references do not provide genotype information.

However, as a show of good faith, the applicant provided additional evidence, in the form of the following two papers, for the purpose of demonstrating how a skilled person would be able to carry out the invention using the clinical data contained in these papers:

(1) "Genotypic and phenotypic analyses of HIV-1 in antretroviral-experienced patients treated with tenofovir DF," Margot, N.A., et al., *AIDS*, 2002, **16**:1227-1235; and

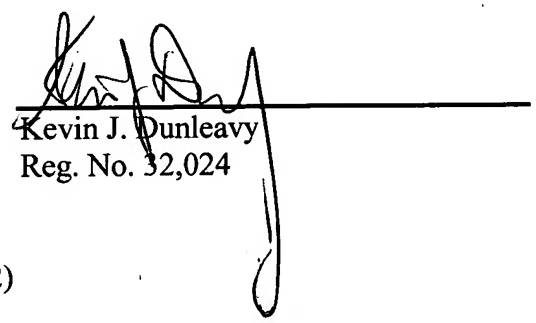
(2) "Clinically relevant interpretation of genotype for resistance to abacavir," Brun-Vézinet, F. et al., *AIDS*, 2003, **17**:1795-1802.

On the basis of these publications, Dr. Boucher described to the Examiner at the personal interview how a skilled person would go about carrying out the invention as claimed.

In view of the foregoing, favorable consideration, withdrawal of the sole outstanding rejection and issuance of a Notice of Allowance are requested.

Date: March 9, 2005

Respectfully Submitted,



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